Title: Cost-effectiveness analysis of Speedboat submucosal dissection in the management of large nonpedunculated colorectal polyps

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Abstract:

Background and aims: Speedboat is a new medical device to perform submucosal dissection in patients with large nonpedunculated colorectal polyps (LNPCP). This study was aimed to assess the early cost-effectiveness of Speedboat in the UK setting.

Methods: Patients were stratified in two subpopulations of benign or malignant lesions. Markov model was applied to describe the course of the disease over a lifetime horizon. For the benign subpopulation, Speedboat submucosal dissection (SSD) was compared to endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Laparoscopic colon surgery (LCS) and ESD were two comparators against SSD in the malignant subpopulation. Costs were valued from the National Health System (NHS) and Personal Social Service. Incremental life-years, quality-adjusted life-years, and cost were estimated for SSD against other comparators. Four clinical outcomes were also considered to estimate the proportion of patients avoided from open surgery, distant recurrence, local recurrence, and procedure-related complications. Ultimately, the cost-effectiveness of Speedboat device was estimated in the total population. Sensitivity and scenario analyses were performed.

Results: In sub- and total populations, Speedboat device dominated other alternatives. Despite an identical cost for EMR, ESD, and SSD in the NHS setting, cost-saving was driven by reducing downstream costs associated with local and distant recurrences as well as procedure-related complications in the SSD arm. SSD was 100% cost-effective compared to the combination of using EMR for benign and LCS for malignant populations. Similarly, SSD showed being cost-effective with a probability of >83% compared to ESD in the total population. Clinical outcomes were improved using Speedboat device and SSD technique. The most improvement, which was the incremental proportion of avoided local recurrence (11.01%), was seen for the comparison of SSD with EMR+LCS.

Conclusion: This study suggests that Speedboat device would be cost-effective compared to other alternatives for the management of LNPCP in the UK. Further studies are considered necessary to ascertain this result.

1. Introduction

Large nonpedunculated colorectal polyps (LNPCP) include benign (or premalignant), and malignant lesions (1). Benign colon tumors, which are common and usually asymptomatic, are mostly colorectal polyps and may be either neoplastic or non-neoplastic (2). The majority of colorectal cancers (CRCs) - a major cause of morbidity and mortality in Western countries – arises from benign precursors along the adenoma-carcinoma sequence (3). The results of previous studies showed that CRC could be prevented by the removal of premalignant polyps (4,5). There are currently two main approaches for colorectal lesion management: endoscopic therapies and laparoscopic colon surgery.

Endoscopic therapies are used for benign and premalignant lesions as well as superficial noninvasive cancers with a low risk of lymph node metastasis. Endoscopic therapies include mainly resection-based modalities. Resection-based modalities include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) (6). The EMR is able to resect lesions with a diameter of less than 20 mm in an en bloc fashion and can resect larger lesions in a piecemeal manner (6). In contrast, ESD facilitates en bloc resection of a lesion irrespective of its size, but most likely lesions with a diameter of more than 20mm (7). A systematic review by Arezzo et al. (2016) showed that the ESD provides a higher rate of en bloc and R0 resection, where there are no cancer cells seen microscopically at the primary site after treatment, compared to EMR (8). However, ESD is associated with higher risks of complications and further surgeries (9).

Laparoscopic colon surgery (LCS) is a minimally invasive procedure that would involve the removal of a segment of the colon. It is an alternative management of the LNPCP following failed endoscopic procedures and a primary treatment for the management of advanced malignant lesions. LCS involves several small incisions to insert a laparoscope, which allows the surgeon to visualize and perform surgery without the large incision required for open surgery. Compared with open surgery, LCS can improve patients' quality of life through improved short-term postoperative results, including less intraoperative blood loss and earlier return to normal bowel function, reduced needs for analgesic consumption, and reduced duration of hospital stay (10–12). Consequently, clinical guidelines, including guidelines from the National Institute of Health and Care Excellence (NICE), recommend the use of LCS as the standard of care in almost all colorectal cancers (7,13). However, there is a 12% chance LCS will require conversion to open surgery (14).

Speedboat device is a novel technology to perform submucosal dissection that uses innovative modalities for cutting and coagulation of the lesion. The results of a case study showed that Speedboat device applying SSD could successfully perform a complete resection of a benign surface lesion (15).

The objective of this study is to investigate an early cost-effectiveness of speedboat device in patients who are candidates for endoscopic therapies in the management of large nonpedunculated colorectal polyps (LNPCPs).

2. Method

A de novo decision-analytic Markov model was developed to estimate the marginal differences in clinical outcomes and healthcare costs of Speedboat device and SSD with other treatment strategies in two groups of patients with LNPCP. A cohort for patients with LNPCP was designed and included the necessary data in the model to estimate the incremental cost-effectiveness ratio (ICER) of using Speedboat device over a lifetime horizon from the National Health System (NHS) and Personal Social Service (PSS) perspective in the UK.

2.1. Patient populations

The model included patients with LNPCP. Patient characteristic obtained from a large meta-analysis on efficacy and safety of endoscopic resection of large colorectal polyps (16). The mean age at start was 67 years (SD=3.82), and 51% of the patients were male (16). Due to heterogeneity among patients who are eligible to receive EMR, LCS, conventional ESD (hereinafter called "ESD") for polyp resection, the target population in the model will be considered as two subpopulations including patients with benign, and patients with superficial malignant colorectal lesions.

The first subpopulation represents those patients that suffer from a benign (non-cancerous) lesion. There is no chance of distant recurrence for benign colorectal lesions however, it is possible that the benign lesions recur after tumor resection (local recurrence). EMR or ESD are the current cure for this group of patients.

The second subpopulation represents patients who might experience distant recurrence (metastasis) as a result of the spread of cancerous cells to tissues distant from the primary tumor location through the blood or lymphatic system. Patients in this subpopulation, therefore, consume more healthcare resources and, on average, experience a lower quality-of-life and/or life expectancy than the first subpopulation. LCS or ESD are being used for the management of patients with superficial malignant colorectal lesions.

The model also allows for the total LNPCP population (both two subpopulations) to be considered as a whole, by using a weighted average of the outputs for the subpopulations.

2.2. Model structure

A model structure was designed based on the patient pathway obtained from NHS clinical guidelines (17,18) and expert opinion (Figure 1). Each subpopulation of patients with LNPCPs entered into the model in LNPCP health state. They might receive one of the current endoscopic procedures (EMR or ESD for benign population and LCS or ESD for superficial malignant population) for tumor resection of colorectal lesions. Speedboat device and SSD were considered to be used in both subpopulations as the main intervention. Following their primary treatment, patients may move into one of four possible states: patients may have a successful procedure and enter into the remission health state, they might need to receive either open or laparoscopic surgery due to any complications or incomplete primary procedure, or they may move into the death state. Patients who had undergone open surgery then moved into either the remission health state or died due to surgery-related complications. Patients who underwent laparoscopic surgery similarly may move into either the remission or death states. However, there is also a chance of unsuccessful laparoscopic surgery in which case patients experience open surgery and then follow the outlined pathway from that state. Patients undergoing endoscopic procedures, laparoscopic surgery, and open surgery may suffer from procedure-related complications; the impact of complications on the costs and health outcomes associated with that patient's pathway was considered in the model.

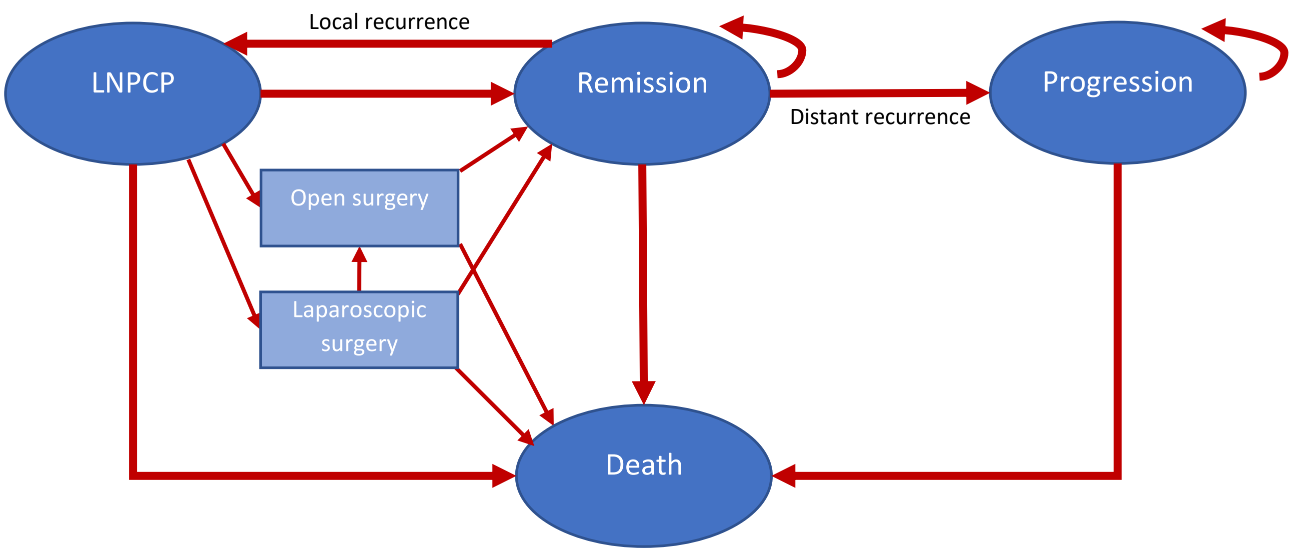

Figure 1: Model structure

When in the remission health state, patients may stay in this health state without experiencing any recurrence or they experienced either local or distant (metastasis) recurrence. Patients who stayed in the remission health state may undergo surveillance according to the British Society of Gastroenterology/Association of Coloproctology of Great Britain and Ireland/Public Health England post-polypectomy and post-colorectal cancer resection surveillance guidelines (17). For EMR (piecemeal procedure), surveillance happened in cycles 1, 2, 6, and 12. For en-bloc procedures (ESD, SSD, and LCS), only one surveillance in cycle 12 was considered. Where patients experienced local recurrence, they re-entered into the LNPCP health state, and they would, once again, be a candidate to receive tumor resection. Switching between strategies for treatment of recurrence was not considered in this study due to lack of data. Patients underwent the same strategy in any further rounds of endoscopic procedures as they did initially. Patients would enter the progression health state if they experienced a distant recurrence (metastasis). Various types of treatment in the management of metastatic colorectal cancer was not considered in this study assuming the same experience for patients in different arms. Patients remained in this health state until they die due to colorectal cancer.

While in any of the health states, there remains a chance of death due to the age-specific background mortality rate.

2.3. Transition probabilities

The following items describe the input parameters used in the model as well as their sources. Different transition probabilities used in the model are shown in Table 1.

2.3.1. Probability of surgery followed by primary procedure

Probability of surgery for EMR was derived from a systematic review and meta-analysis of 11 studies which compared clinical outcomes of EMR and ESD (8). For ESD, we used the results of another systematic review and meta-analysis on the results of 50 studies regarding the efficacy and safety of endoscopic resection of large colorectal polyps (16).

Patients who should undergo surgery, were distributed between laparoscopic surgery and open surgery. The proportion of patients who underwent laparoscopic surgery was obtained from the National Bowel Cancer Audit (NBOCA) report. For EMR, ESD, and SSD, we used the overall ratio between laparoscopic surgery and open surgery. However, for LCS, we looked at the proportion of patients who needed re-operation following a completed laparoscopic surgery (n=644) among all who underwent laparoscopic surgery (n=2041).

2.3.2. Probability of recurrence

The probability of local and distant recurrences varied depending on whether patients received an endoscopic procedure alone or in combination with surgery. Therefore, patients in the remission health state were proportionally distributed based on their service received, and different probabilities of recurrences were applied for each treatment/combination of treatments.

2.3.2.1. Probabilities of local recurrence

For EMR, and ESD (both subpopulations), the probabilities of local recurrence were obtained from a systematic review and meta-analysis over a two-year follow-up period (16). A weighted average of the local recurrence rates in five included studies in a systematic review by Furne´e et al. 2017 was used to estimate the local recurrence probability followed by LCS over a 2.8 year follow-up period (19).

Table1: Input parameters, general parameters, and transition probabilities

Input parameters	Value	Lower	Upper		Source
			General parameters		
Benefit Discount Rate	3.5%	1.5%	6.0%		NICE guideline for economic evaluations
Costs Discount Rate	3.5%	1.5%	6.0%		NICE guideline for economic evaluations
Age	67.00	66	68		Hassan 2016
Proportion male	0.51	0.49	0.52		Hassan 2016
Proportion of patient population with benign lesions	0.80	0.64	0.96		Assumption
			Transition probabilities: Benign lesions		
Probability of surgery (per cycle)					
EMR	3.01%	1.92%	4.33%	95% CI	Arezzo 2015
ESD	7.90%	3.00%	20.80%	95% CI	Hassan 2016
SSD	3.95%	1.50%	10.40%	95% CI	Assumption (A relative risk of 50% vs ESD)
Laparoscopic surgery	17.62%	16.93%	18.32%	95% CI	The National Bowel Cancer Audit (NBOCA)
% Laparoscopic surgery					
EMR	70.50%	69.80%	71.20%	95% CI	The National Bowel Cancer Audit (NBOCA)
ESD	70.50%	69.80%	71.20%	95% CI	The National Bowel Cancer Audit (NBOCA)
SSD	70.50%	69.80%	71.20%	95% CI	Assumption
Probability of recurrence					
Local recurrence after EMR (2 years)	15.13%	14.13%	16.15%	95% CI	Hassan 2016
Local recurrence after ESD (2 years)	0.86%	0.28%	1.76%	95% CI	Hassan 2016
Local recurrence after SSD	0.43%	0.34%	0.52%	95% CI	Assumption (A relative risk of 50% vs ESD)
Local recurrence after surgery	0.00%			-	Assumption
Probability of death					
Death due to laparoscopic surgery	0.01	0.01	0.02	95% CI	Allaix 2016
Death due to laparoscopic surgery followed by open surgery	0.03	0.01	0.05	95% CI	Allaix 2016
Death due to open surgery	0.02	0.02	0.03	95% CI	Hureibi 2018
Procedure side-effect - perforation					
EMR	0.40%	0.11%	0.86%	95% CI	Cipolletta 2013
ESD	1.09%	0.72%	1.64%	95% CI	Arezzo 2015
SSD	0.55%	0.36%	0.82%	95% CI	Assumption (A relative risk of 50% vs ESD)
Procedure side-effect - Bleeding					
EMR	7.61%	6.06%	9.32%	95% CI	Cipolletta 2013
ESD	5.25%	3.42%	8.07%	95% CI	Arezzo 2015
SSD	1.31%	0.86%	2.02%	95% CI	Assumption (A relative risk of 25% vs ESD)
			Transition probabilities: Superficial Malignant lesions		
Probability of surgery (per cycle)					
LCS (primary)	12.06%	11.47%	12.66%	95% CI	The National Bowel Cancer Audit (NBOCA)
ESD	7.90%	3.00%	20.80%	95% CI	Hassan 2016
SSD	3.95%	1.50%	10.40%	95% CI	Assumption (A relative risk of 50% vs ESD)

Laparoscopic surgery (secondary)	6.82%	6.37%	7.29%	95% CI	The National Bowel Cancer Audit (NBOCA)
% Laparoscopic surgery					
LCS	31.55%	29.55%	33.59%	95% CI	The National Bowel Cancer Audit (NBOCA)
ESD	70.50%	69.80%	71.20%	95% CI	The National Bowel Cancer Audit (NBOCA)
SSD	70.50%	69.80%	71.20%	95% CI	Assumption
Probability of recurrence					
Local recurrence after LCS (primary) (2.8 years)	6.75%	3.27%	11.37%	95% CI	Furne´e 2017
Local recurrence after ESD (2 years)	0.86%	0.28%	1.76%	95% CI	Hassan 2016
Local recurrence after SSD	0.43%	0.14%	0.88%	95% CI	Assumption (A relative risk of 50% vs ESD)
Local recurrence after surgery	0.82%	0.53%	1.18%	95% CI	Wang 2009
Distant recurrence after LCS (primary) (per cycle)	1.08%	0.63%	1.66%	95% CI	Furne´e 2017
Distant recurrence after ESD	0.10%	0.03%	0.22%	95% CI	Tamaru 2017
Distant recurrence after SSD	0.10%	0.03%	0.22%	95% CI	Tamaru 2017
Distant recurrence after surgery	0.23%	0.09%	0.44%	95% CI	Wang 2009
Probability of death					
Death due to laparoscopic surgery	1.10%	0.76%	1.51%	95% CI	Allaix 2016
Death due to laparoscopic surgery followed by open surgery	2.53%	1.10%	4.53%	95% CI	Allaix 2016
Death due to open surgery	2.47%	1.98%	2.96%	95% CI	Hureibi 2018
Death due to cancer (per cycle)	4.27%	4.09%	4.44%	95% CI	The National Bowel Cancer Audit (NBOCA)
Procedure side-effect - perforation					
Laparoscopic surgery	2.00%	0.55%	4.34%	95% CI	Scala 2006
ESD	1.09%	0.72%	1.64%	95% CI	Arezzo 2015
SSD	0.55%	0.36%	0.82%	95% CI	Assumption (A relative risk of 50% vs ESD)
Procedure side-effect - Bleeding					
Laparoscopic surgery	1.00%	0.12%	2.77%	95% CI	Scala 2006
ESD	5.25%	3.42%	8.07%	95% CI	Arezzo 2015
SSD	1.31%	0.86%	2.02%	95% CI	Assumption (A relative risk of 25% vs ESD)

Probability of local recurrence after SSD were assumed equal to 50% of rates for ESD in both benign and superficial malignant populations.

Hassan et al. (2016) mentioned that most cases with local recurrence happened in the early phase (80%) (16). Therefore, we used an exponential cumulative distribution function (1-exp($\lambda \times t_i$)), in which 80% of cases happened in the first six months after the primary treatment (λ = 0.805) for any intervention.

For the benign subpopulation, we assumed that there is no risk of local recurrence after surgery. The local recurrence probability after surgery for the superficial malignant subpopulation was derived from a study by Wang et al. 2009 examining the long-term consequences of postoperative colorectal cancer (average follow-up = 24.8 months by pooling results from both arms (20).

2.3.2.2. Probabilities of distant recurrence

The probability of distant recurrence for LCS was obtained by estimating a weighted average of the results of five included studies by Furne´e et al. 2017 (19).

We could not find any study that explicitly investigated the long-term impact of ESD during our targeted search on the probability of distant recurrence. A study by Tamaru et al. 2017 examined long-term outcomes after endoscopic resection for T1 colorectal carcinoma over an average follow-up period of 100.8 months. The included endoscopic resections in this study were polypectomy, EMR, and ESD. In the lack of data, we used the results of Tamaru et al. 2017 (group A) to estimate the probability of distant recurrent after ESD and SSD (21).

The probability of distant recurrence after surgery was derived from the study by Wang et al. 2009 (20).

2.3.3. Procedure complications

Two important complications (perforation and bleeding) due to EMR, ESD, and LCS were included in the model. Although other complications may be expected for LCS, we did not include other complications because of the difficulties in obtaining disutilities associated with most of the additional complications.

Two studies by Cipolletta et al. 2013 (22) and Arezzo et al. 2016 (8) were used to obtain the probabilities of perforation and bleeding due to EMR and ESD, respectively. According to expert opinion, we assumed a relative risk of 50% and 25% for perforation and bleeding for SSD compared to ESD, respectively. Scala et al. 2007 were used to estimate the probabilities of perforation and bleeding after LCS (23).

2.3.4. Mortality.

Different types of mortality rates were considered in the model. Firstly, the background mortality rate was identified using the latest version of age- and sex-specific death rates in the general population in England & Wales (national life table) (24). For each age group, the probability of death was estimated using the sex ratio in the population of interest obtained from Cipolletta et al. 2013 (22). Secondly, the probabilities of death due to LCS, LCS followed by open surgery, and open surgery were considered in the model. These three probabilities were identical between benign and malignant populations. We used Allaix et al. 2016 to obtain probabilities of death after LCS and LCS followed by open surgery (25). For probability of death due to open surgery, the results of Hureibi et al. 2018 were applied in the model (26). Finally, we included probability of death due to colorectal cancer for the malignant subpopulation which was obtained from NBOCA (14).

We assumed that there is no chance of death associated with EMR, ESD, and Speedboat.

2.4. Outcomes

Two series of health economics outcomes (Life-years (LYs), and quality-adjusted life-years (QALYs)) and clinical outcomes consist of a) the proportion of open surgery avoided, b) the proportion of distant recurrence avoided c) the proportion of local recurrences avoided and d) the proportion of procedure-related complications avoided were estimated for all procedures.

Table 2 shows the utility values used in this study. We used the results of a study that provided the utility weights for various health states in the first line of management of colorectal cancer (27). Another study that used the EQ-5D values was selected to find the utility weight for patients who underwent laparoscopic surgery and open surgery (18). Finally, the disutility values (EQ-5D) for patients who suffered from the perforation and bleeding were obtained from studies by Whyte et al. 2017 (28) and Huxley et al. 2017 (29), respectively. We considered complication duration of two weeks and one month for bleeding and perforations, respectively.

2.5. Costs

An identical cost of £782.97 was considered for EMR, ESD, and SSD, according to the National Schedule of Reference Costs (NSRC) (2018-19) (30). To do so, we estimated the weighted average of the day case unit costs for codes FE02A-F. We also used the NSRC data to estimate the costs of laparoscopic surgery using unit costs for elective surgery (codes FF33A-B). Unit costs for elective open surgeries (codes FD10A-D and FD11A-D) were used for open surgeries in benign and malignant subpopulations, respectively. Costs associated with perforation and bleeding were derived from Whyte et al. 2011 (28).

Costs associated with cancer management in the malignant subpopulation were obtained from a cost-effectiveness of improving early diagnosis (31). We considered the cost to treat stages 1 and 4 for the remission and the progression health states, respectively.

Costs obtained from the literature were inflated to the costs in 2019 using the Health Services index (32).

Table1: Input parameters, health utilities and costs

Input parameters	Value	Lower	Upper		Source
			Health utilities		
Utility values					
LNPCP (Endoscopic procedures)	0.84	0.81	0.87	95% CI	Ewara 2014
Remission	0.84	0.81	0.87	95% CI	Ewara 2014
Progression	0.68	0.65	0.71	95% CI	Ewara 2014
Laparoscopic surgery	0.83	0.80	0.86	95% CI	Jordan 2014
Open surgery	0.82	0.78	0.85	95% CI	Jordan 2014
Disutility values					
Bleeding	0.006	0.005	0.01	±20%	Whyte 2017
Perforation	0.049	0.039	0.23	±20%	Huxley 2017
			Health Resource Utilization		
			Costs: Benign lesions		
Costs of endoscopic procedure (NHS)					
EMR	£ 783	£ 769	£ 797	95% CI	NSRCY 2018-19
ESD	£ 783	£ 769	£ 797	95% CI	NSRCY 2018-19
SSD	£ 783	£ 769	£ 797	95% CI	NSRCY 2018-19
Costs of surgery services					
Cost of laparoscopic surgery	£ 6,536	£ 6,502	£ 6,571	95% CI	NSRCY 2018-19*
Cost of open surgery	£ 5,465	£ 5,206	£ 5,731	95% CI	NSRCY 2018-19*
Costs of complications					
Bleeding	£ 459	£ 321	£ 596	±30%	Whyte 2011
Perforation	£ 3,787	£ 2,651	£ 4,923	±30%	Whyte 2011
			Costs: Malignant lesions		

Costs of procedures (NHS)					
LCS (primary)	£ 6,536	£ 6,502	£ 6,571	95% CI	NSRCY 2018-19
ESD	£ 783	£ 769	£ 797	95% CI	NSRCY 2018-19
SSD	£ 783	£ 769	£ 797	95% CI	NSRCY 2018-19
Costs of surgery services					
Cost of laparoscopic surgery	£ 6,294	£ 6,247	£ 6,340	95% CI	NSRCY 2018-19
Cost of open surgery	£ 5,944	£ 5,404	£ 6,509	95% CI	NSRCY 2018-19
Costs of disease management (per cycle)					
In remission health state (excluding surveillance)	£ 1,038	£ 727	£ 1,349	±30%	PHE 2016
In progression health state	£ 5,136	£ 3,595	£ 6,676	±30%	PHE 2016
Costs of complications					
Bleeding	£ 459	£ 321	£ 596	±30%	Whyte 2011
Perforation	£ 3,787	£ 2,651	£ 4,923	±30%	Whyte 2011

2.6. Analysis

Both costs and outcomes were discounted by 3.5% per annum as suggested by the NICE guideline (33). A half-cycle correction was also applied. We performed the cost-effectiveness analyses for two subpopulations as well as the total population. A willingness-to-pay (WTP) of £20,000 per QALY was considered in the analysis.

The impact of specific input parameters on the net monetary benefit (NMB) of cost-effectiveness analyses was examined using deterministic sensitivity analysis (DSA). The ranges in values were determined based on the literature (95% confidence interval (CI)) or expert opinion. Probabilistic sensitivity analyses (PSAs) was performed to quantify the overall uncertainty in the expected output measures. The gamma distribution was applied for costs. The beta distribution was used for binomial proportions and utility weights. The PSAs used 5,000 iterations obtained via Markov Chain Monte Carlo simulation.

2.7. Scenario analysis

Due to the importance of surgery rate in the analysis, in the lack of robust data, we conducted a scenario in which an identical probability of surgery was used for both ESD and SSD. In this scenario, we looked at the changes in NMB and the probability of being cost effective for SSD.

3. Results

Speedboat device and SSD is cost-effective over a lifetime horizon compared to other comparators at a WTP of £20,000/QALY (Table 3). The results of PSA, shown in Figure 2, show that at the WTP threshold of £20,000/QALY, Speedboat device and SSD with 100% and >83% probabilities is more cost-effective versus a combination of EMR + LCS (using in the corresponding subpopulation) and ESD, respectively. The results of PSA for subpopulations are shown in Appendices 1 and 3.

Table 3: the results of cost-effectiveness analyses (base-case) for sub populations and total population

Population	Procedures	LYs	QALYs	Costs	ICER (QALY)	NMB
Benign	SSD	13.14	11.04	£1,765		
	EMR	13.15	11.02	£4,132	NA	NA
	ESD	13.13	11.02	£2,080		
	SSD vs EMR	*0.00*	*0.01*	*-£2,367*	*Dominate*	*£2,611*
	SSD vs ESD	*0.01*	*0.02*	*-£315*	*Dominate*	*£671*
Malignant	SSD	12.86	10.77	£9,874		
	LCS	12.23	10.19	£21,809	NA	NA
	ESD	12.84	10.74	£10,190		
	SSD vs LCS	*0.64*	*0.57*	*-£11,934*	*Dominate*	*£23,395*
	SSD vs ESD	*0.02*	*0.03*	*-£315*	*Dominate*	*£873*
Total population	SSD	13.09	10.98	£3,387		
	EMR + LCS	12.96	10.86	£7,668	NA	NA
	ESD	13.08	10.96	£3,702		
	SSD vs EMR + LCS	*0.13*	*0.12*	*-£4,280*	*Dominate*	*£6,768*
	SSD vs ESD	*0.01*	*0.02*	*-£315*	*Dominate*	*£712*

The results of the DSA are shown in Figure 3. The main key drivers of the model results were the probabilities of distant recurrence for Speedboat and comparators. Moreover, the proportion of benign patients was the key driver when the comparator was the combination of EMR and LCS. However, the probabilities of surgery for ESD had a considerable impact on NMB when it was SSD's comparator. The results of DSA for subpopulations are shown in Appendices 2 and 4.

The scenario analysis (identical probability of surgery for ESD and SSD), led to an incremental QALYs of 0.01 and a cost-saving of £42. Therefore, Speedboat still dominates ESD with an NMB equal to £239 with a probability of 65%.

Table 4 shows the results of the model regarding clinical outcomes. SSD showed better outcomes than other procedures except for reducing the chance of surgery compared with EMR due to a higher probability of perforation in the SSD arm. However, SSD could reduce the overall chance of procedure-related complications due to the lower probability of bleeding compared to EMR.

In the superficial malignant subpopulation, SSD could reduce the chance of open surgery by 7.74% comparing to LCS. Moreover, SSD showed a considerable impact on the reduction in the chance of local recurrence (on average, 8.25%) in both subpopulations.

Table 4: the results of model for clinical outcomes (base-case) for sub populations and total population

Populations	Procedures	% Open surgeries avoided	% Distant recurrences avoided	% Local recurrence avoided	% Patients without procedure-related complications
Benign	SSD	98.34%	100.00%	99.66%	98.14%
	EMR	98.67%	100.00%	87.96%	91.57%
	ESD	96.68%	100.00%	99.33%	93.64%
	SSD vs EMR	*-0.33%*	*0.00%*	*11.69%*	*6.57%*
	SSD vs ESD	*1.66%*	*0.00%*	*0.33%*	*4.50%*
Malignant	SSD	98.62%	97.86%	98.17%	98.11%
	LCS	90.89%	92.42%	89.92%	96.79%
	ESD	97.20%	97.80%	93.52%	93.44%
	SSD vs LCS	*7.74%*	*5.45%*	*8.25%*	*1.32%*
	SSD vs ESD	*1.43%*	*0.07%*	*4.65%*	*4.67%*
Total	SSD	98.40%	99.57%	99.36%	98.13%
	EMR + LCS	97.11%	98.48%	88.36%	92.62%
	ESD	96.78%	99.56%	98.17%	93.60%
	SSD vs EMR + LCS	*1.28%*	*1.09%*	*11.01%*	*5.52%*
	SSD vs ESD	*1.62%*	*0.01%*	*1.19%*	*4.53%*

4. Discussion

Endoscopic resections are widely used to remove colorectal lesions as a cost-effective and less invasive alternative to surgery (34). Methods for endoscopic resections are improved over time to increase the performance (such as higher R0 resection rate) and reduce procedure-related complications. Speedboat device, the first advanced energy instrument designed for use in flexible endoscopy, could be an option to achieve a better rate of clinical responses and a considerable reduction in complication rate according to the results of a primary study on efficacy and safety of Speedboat device and SSD (9). Our study was aimed to explore an early assessment regarding the cost-effectiveness of Speedboat compared to other routine alternatives in the UK.

The results of our model-based study show that Speedboat device and SSD would be cost-effective compared to other routine alternatives. From an NHS and PSS perspective, Speedboat device has the potential to be a cost-saving procedure that is possibly more effective and safer than the conventional ESD and EMR in both subpopulations. In the superficial malignant subpopulation, SSD can be even more efficient than LCS due to the lower rate of distant recurrence, which leads to more gained life-years. Overall, Speedboat device could potentially reduce downstream costs, specifically in the superficial malignant population.

To our knowledge this is the first study that assessed the cost-effectiveness of endoscopic procedures by stratifying the patient population into two groups of low and high-risk of colorectal cancer progression. This stratification approach facilitated inclusion of different comparators in the analysis based on their clinical indications. Moreover, we could better capture the long-term clinical outcomes as well as downstream costs associated with cancer management.

There are some study limitations worth noting. First, we had to rely on the expert opinion on Speedboat device and SSD clinical advantages compared to ESD. There is no available clinical trial for Speedboat device, which resulted in uncertainty about its superiority or inferiority compared to conventional ESD. Despite the importance of this matter, it may not change the interpretation of the results. ESD and SSD apply the same technique for lesion resection, and in many aspects, these two procedures work similarly. Therefore, if ESD has shown more superiority to EMR and LCS, according to the previous publications, it would apply to Speedboat device. Moreover, among those used input parameters based on expert opinion, the results of DSA showed that the probability of surgery would be a key driver in this cost-effectiveness analysis. Thus, in a conservative approach, we examined a scenario considering an identical probability of surgery for both ESD and SSD. As explained in the results section, Speedboat device and SSD, in this scenario analysis, is more cost-effective with a probability of 69% compared to ESD in the total population. Second, the model does not exhaustively capture LCS complications. This is due to lack of relevant data for the management costs and utility decrements associated with LCS complications. Therefore, there is a chance that we underestimated costs and overestimated QALYs gained associated with LCS in this model. Nevertheless, LCS is dominated by SSD, and the interpretation of the model results would remain unchanged if we could include LCS complications exhaustively. Third, while it is expectable that patients undergo en-bloc procedures followed by unsuccessful management with a less invasive procedure in the secondary endoscopic resections, switching between procedures was not included in the model in the absence of reliable information.

Further studies would help to reduce the uncertainty about the effectiveness and cost–effectiveness of Speedboat device. These studies should investigate the long-term efficacy, safety and costs of Speedboat device and SSD versus alternative procedures as well as switching pattern for the secondary endoscopic resections.

5. Conclusion

Endoscopic resections in the management of LNPCP is recognized as first-line therapy internationally. This study estimated the economics and clinical advantages of Speedboat device and SSD, a new device for performing the submucosal dissection. The results lead to the conclusion that the management of LNPCP with Speedboat device appears to be more cost-effective than other alternatives in the UK. However, further studies are necessary to obtain robust conclusions on the cost-effectiveness of Speedboat device.

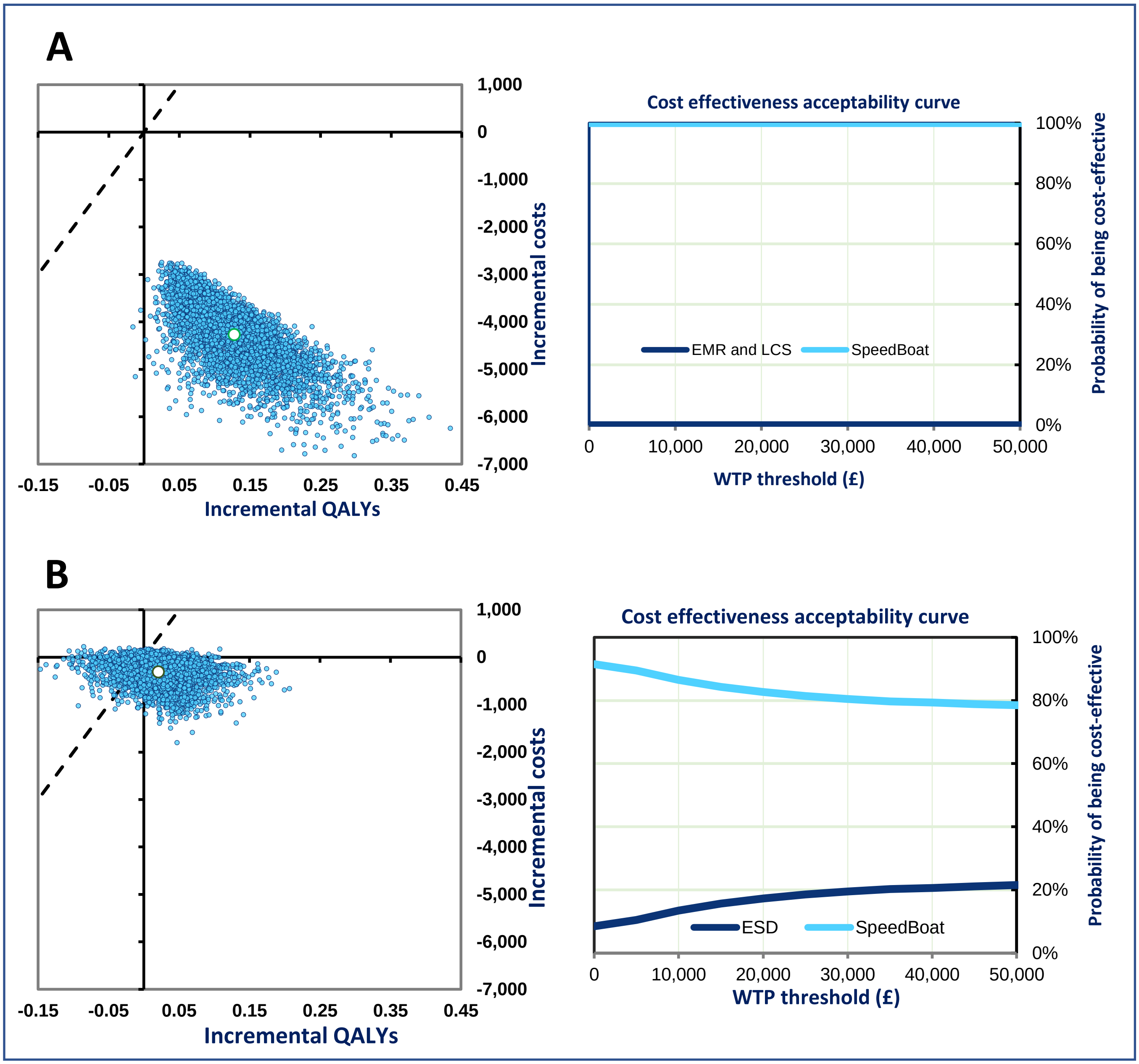

Figure 2: the results of PSA for Speedboat vs **A)** EMR and LCS **B)** ESD in total population over a lifetime horizon

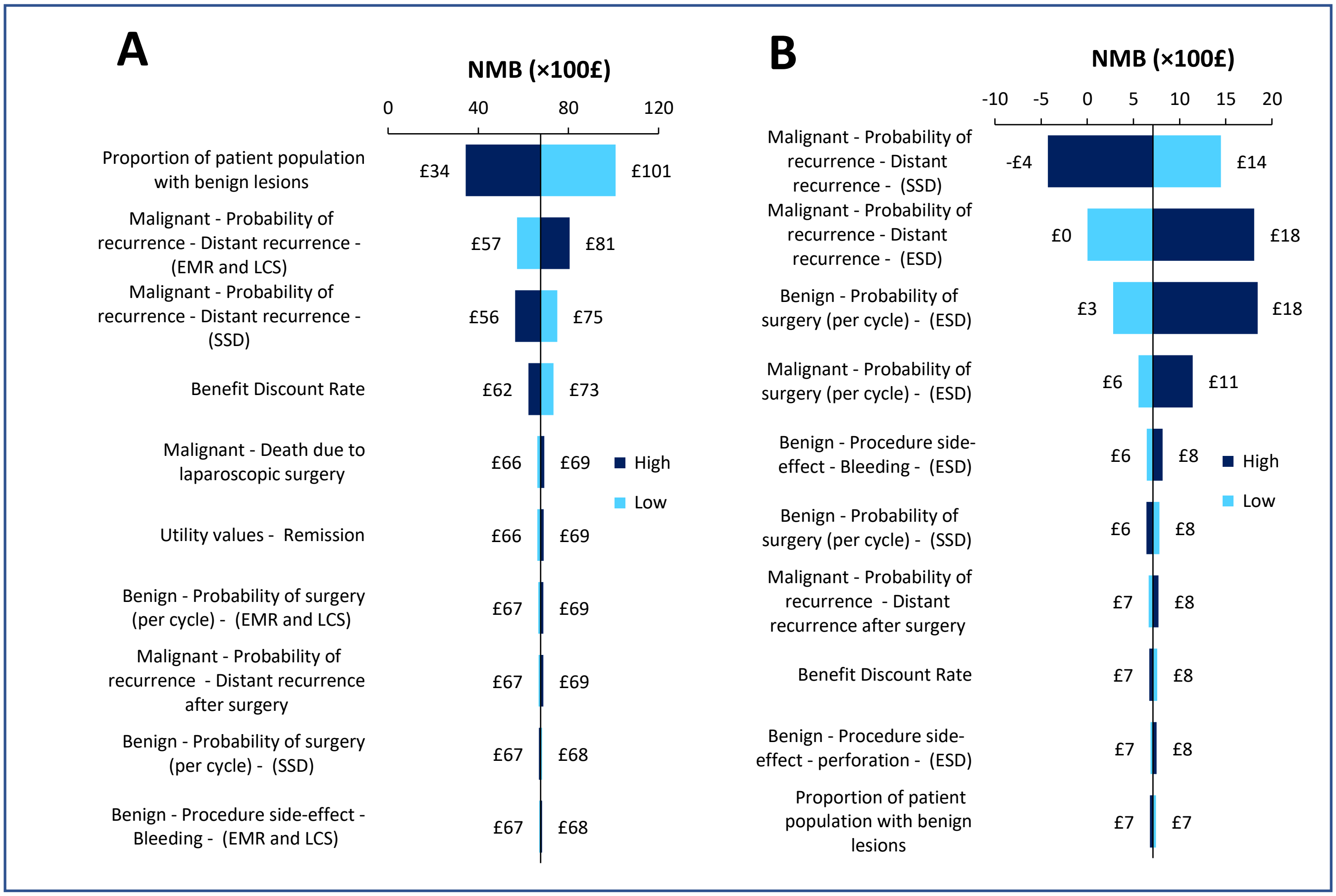

Figure 3: The results of DSA for Speedboat vs **A)** EMR and LCS **B)** ESD in total population over a lifetime horizon

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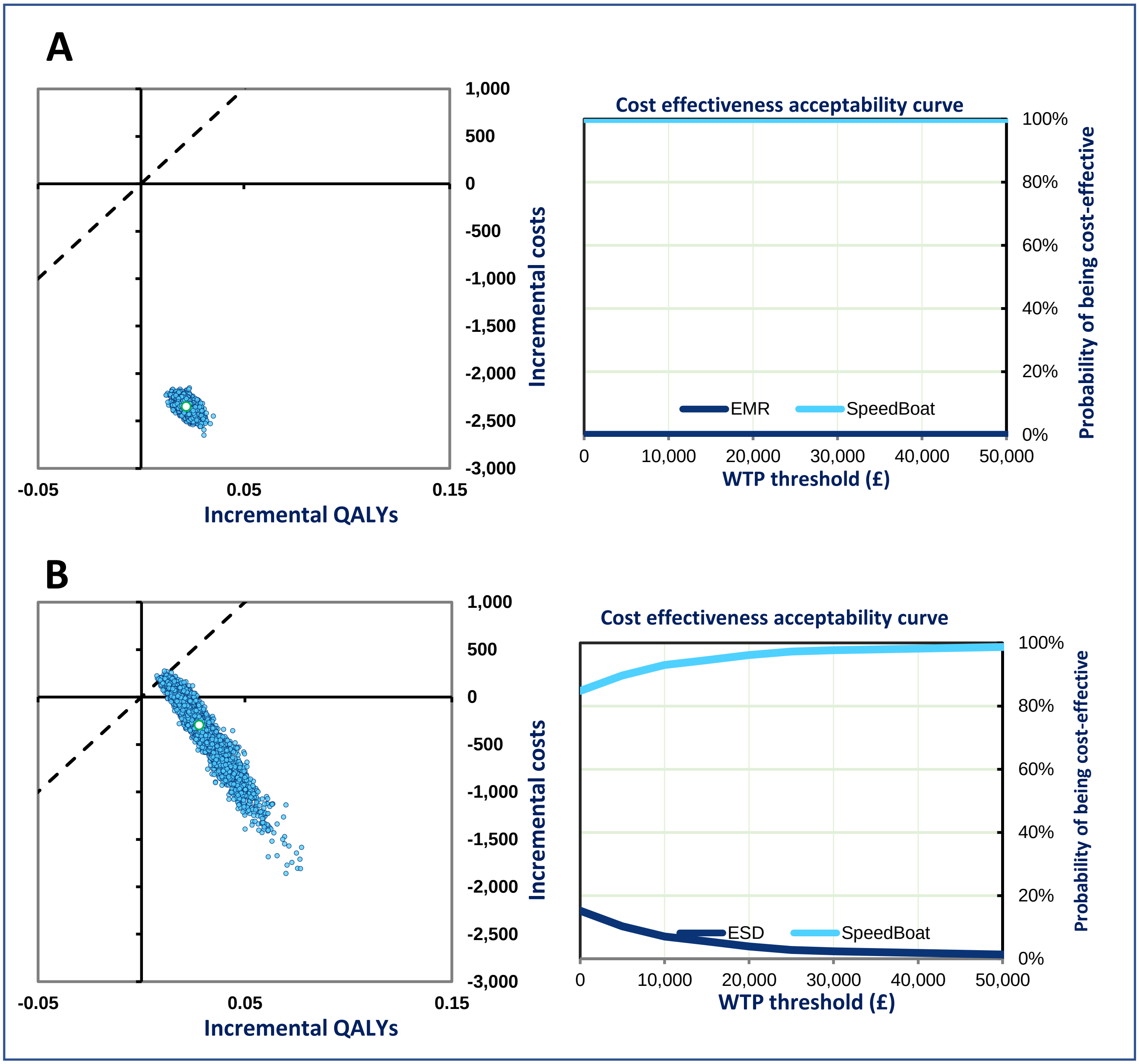
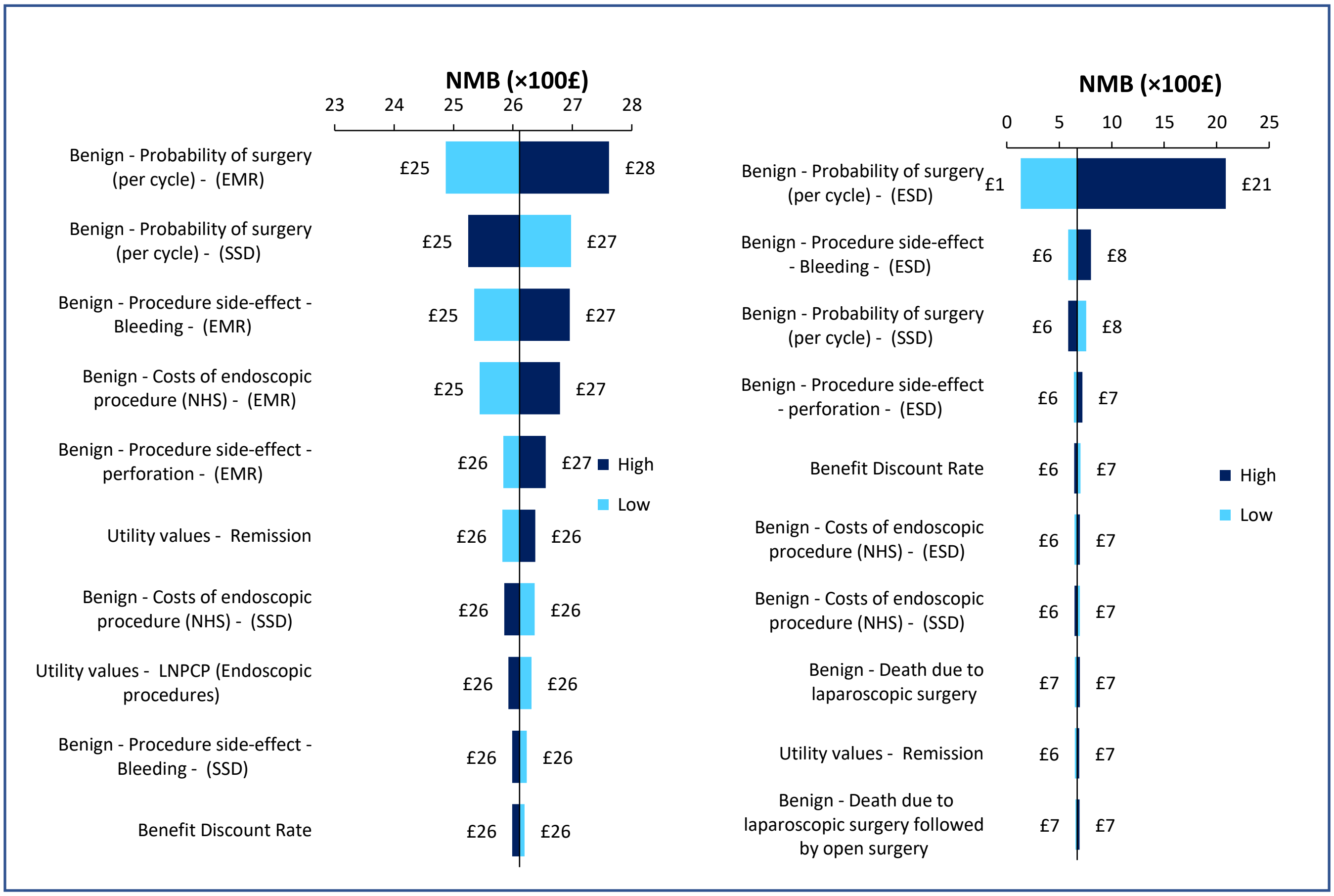
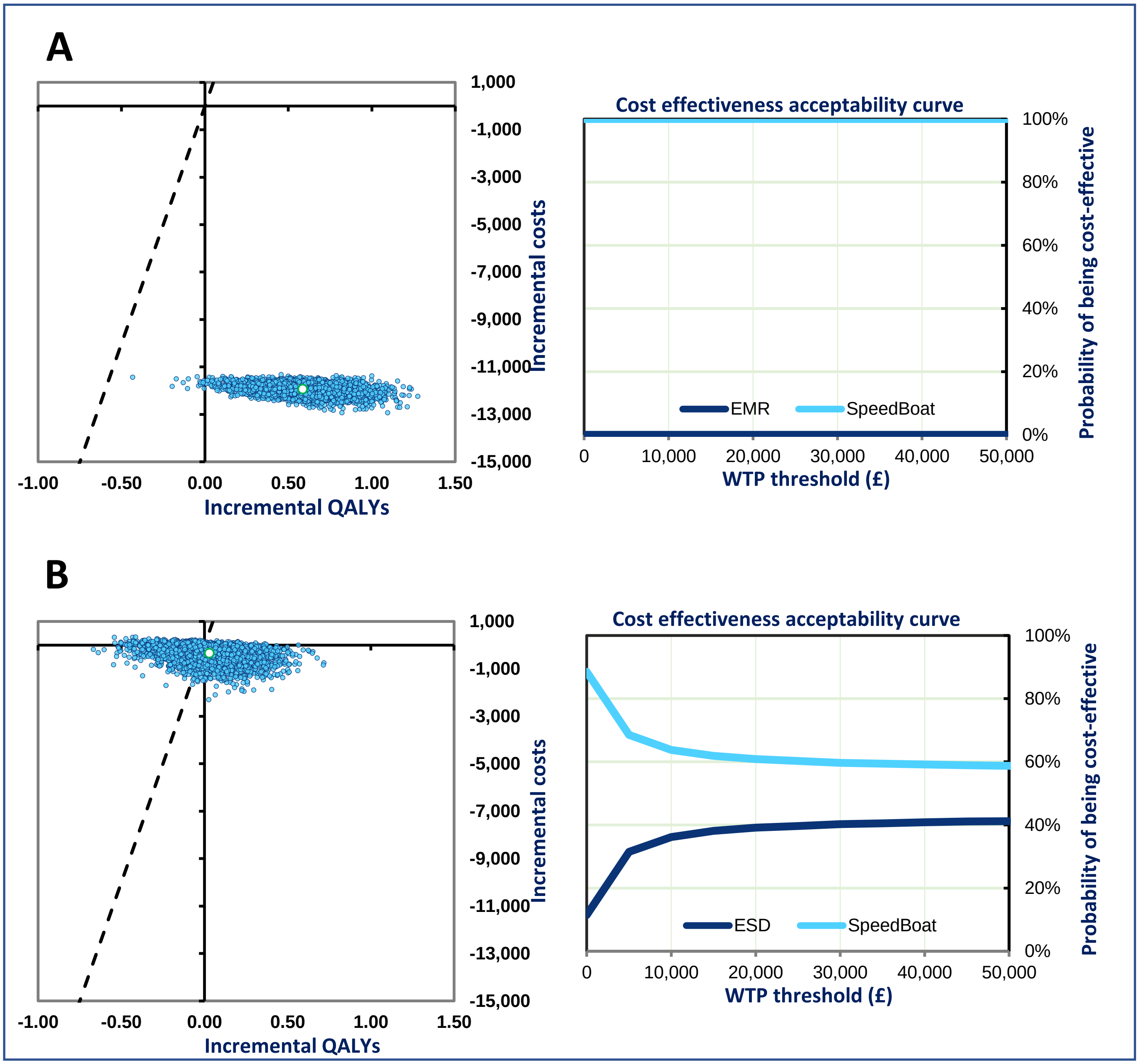


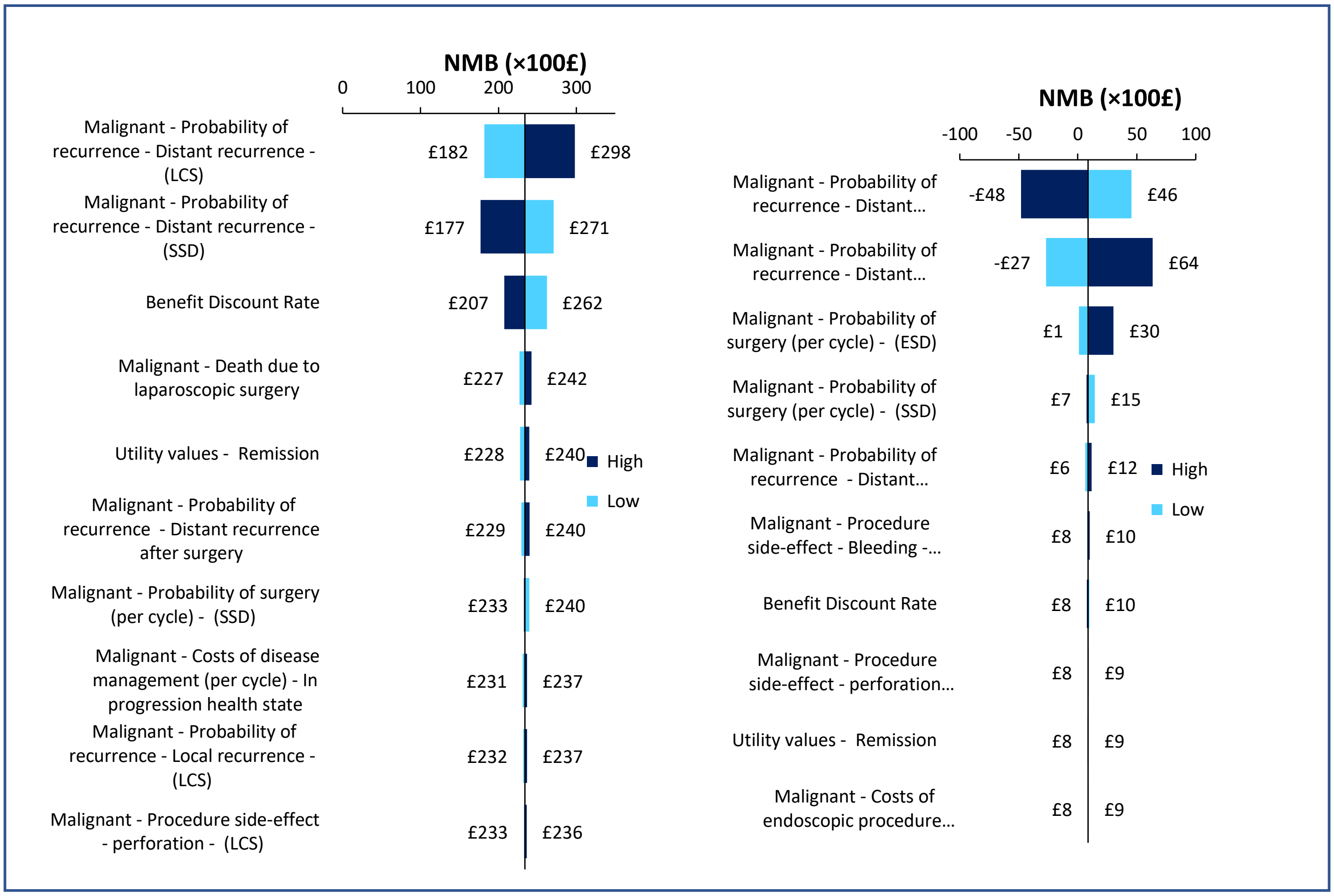
Appendix 1: the results of PSA for Speedboat vs **A)** EMR and **B)** ESD in the benign population over a lifetime horizon



Appendix 2: The results of DSA for Speedboat vs **A)** EMR **B)** ESD in total population over a lifetime horizon



Appendix 3: the results of PSA for Speedboat vs **A)** LCS and **B)** ESD in the malignant population over a lifetime horizon



Appendix 4: The results of DSA for Speedboat vs **A)** LCS and **B)** ESD in total population over a lifetime horizon